

**REMARKS**

Applicant requests reconsideration of the present application, in view of the foregoing amendments and the following remarks.

***I. Introduction***

Claims 1-7, 9-11, 14-26, 30-38 and 41-49 are pending. Claims 8, 12, 13, 27, 28, 39 and 40 have been cancelled without prejudice or disclaimer to expedite prosecution. Claims 41-49 have been added. Claims 41-47 essentially correspond to claims 8, 12, 13, 27, 28, 39 and 40, respectively.

In claim 41, applicant revises " $\text{Ca}_3(\text{PO}_4)_2x\text{H}_2\text{O}$ " of claim 8 to refer to " $\text{Ca}_3(\text{PO}_4)_2(\text{H}_2\text{O})x$ ," as suggested by the examiner. In claims 42 and 43, applicant revises a typographical error in the formula of claims 12 and 13 to recite  $[(\text{PP})(\text{CP})_8]_n$ , along with the revision of "a phosphopeptide" to "said phosphopeptide." Support for the revision is found at page 4, lines 22-24 of the specification. Claims 44-49 reflect the examiner's suggestions on the amendments of the original claims 27, 28, 39 and 40.

Claims 1, 4, 7, 9-11, 15 and 25 have been amended as suggested by the examiner. Applicant notes that while indicating withdrawal of claim 1 from consideration in the office action, the examiner provides applicant with options of either amending or canceling claim 1. According to the examiner's suggestion, applicant has amended claim 1 to recite that calcium fluoride phosphate or the derivative thereof is alkaline. Support of this amendment can be found at page 13, Example 1(B). In this regard, applicant respectfully requests the examiner to clarify the position of claim 1 in this case. Once the amended claim 1 is considered, applicant wishes to add claims that are dependent from claim 1.

Claims 25, 27 and 28 have been withdrawn from the consideration as non-elected subject matter. However, since the amended claim 25, new claims 43 and 44 are now dependent from claim 7, applicant submits that these claims should be examined together with claim 7.

Applicant also resubmits an abstract as a separate sheet following the examiner's request. A revised Sequence Listing to comply with 37 CFR §§1.821-1.825 is submitted concurrently herewith.

**II. Rejections under 35 USC §112, First and Second Paragraphs**

The examiner has rejected claims 39-40 as non-enabled. Without acquiescing to the propriety of the examiner's rejection, applicant has cancelled claims 39-40 and added claims 45-49 to reflect the examiner's suggestions. In this regard, applicant recites "a dentifrice" instead of "delivery vehicle" in claims 46 and 47. Support of this recitation is found at page 5, lines 6-9 of the specification.

Accordingly, applicant respectfully submits that the enablement rejection becomes moot in view of the amendments of claims.

The examiner also has rejected claims 7-16 and 39-40 as indefinite for various reasons. While not acquiescing to the position in the examiner's rejection, applicant has amended the rejected claims as suggested by the examiner, and thus the revisions renders all the indefiniteness rejections moot.

Accordingly, applicant respectfully requests withdrawal of all the rejections.

In view of the foregoing, applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if there are any issues that the Examiner believes could be resolved through a further exchange.

Respectfully submitted,

Date 26 November 2001

By S.A. Bent

FOLEY & LARDNER  
Washington Harbour  
3000 K Street, N.W., Suite 500  
Washington, D.C. 20007-5109  
Telephone: (202) 672-5404  
Facsimile: (202) 672-5399

Stephen A. Bent  
Attorney for Applicant  
Registration No. 29,768

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Marked up replacement paragraph:

Preliminary investigations determined that tryptic casein phosphopeptides contributed to the anticariogenic activity and this was made subject of US Patent No. 5,015,628. In particular, peptides Bos  $\alpha_{s1}$ -casein X-5P (f59-79) (SEQ ID NO: 1), Bos  $\beta$ -casein X-4P (f1-25) (SEQ ID NO: 2), Bos  $\alpha_{s2}$ -casein X-4P (f46-70) (SEQ ID NO: 3) and Bos  $\alpha_{s2}$ -casein X-4P (f1-21) (SEQ ID NO: 4) were disclosed in US Patent 5,015,628 as follows:

(SEQ ID NO: 1) Gln<sup>59</sup>-Met-Glu-Ala-Glu-Ser(P)-Ile-Ser(P)-Ser(P)-Glu-Ile-Val-Pro-Asn-Ser(P)-Val-Glu-Gln-Lys<sup>79</sup>.  $\alpha_{s1}$ (59-79)

(SEQ ID NO: 2) Arg<sup>1</sup>-Glu-[Leu]Leu-Glu-[Iu]Glu-Leu-Asn-Val-Pro-Gly-Glu-Ile-Val-Glu-Ser(P)-Leu-Ser(P)-Ser(P)-Glu-Glu-Ser-Ile-Thr-Arg<sup>25</sup>.  $\beta$ (I-25)

(SEQ ID NO: 3) Asn<sup>46</sup>-Ala-Asn-Glu-Glu-Tyr-Ser-Ile-Gly-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser(P)-Ala-Glu-Val-Ala-Thr-Glu-Glu-Val-Lys<sup>70</sup>.  $\alpha_{s2}$ (46-70)

(SEQ ID NO: 4) Lys<sup>1</sup>-Asn-Thr-Met-Glu-His-Val-Ser(P)-Ser(P)-Glu-Glu-Ser-Ile-Ile-Ser(P)-Gln-Glu-Thr-Tyr-Lys<sup>21</sup>.  $\alpha_{s2}$ (1-21)

Marked up rewritten claims:

1. A stable calcium phosphate complex [including] comprising phosphopeptide-stabilized amorphous calcium fluoride phosphate or a derivative thereof wherein said phosphopeptide includes the amino acid sequence Ser(P)-Ser(P)-Ser(P)-Glu-Glu (SEQ ID NO: 5) and calcium fluoride phosphate or the derivative thereof is alkaline.

4. A complex according to claim 3 wherein said phosphopeptide includes an amino acid sequence selected from [any one] the group consisting of:

(SEQ ID NO: 1) Gln<sup>59</sup>-Met-Glu-Ala-Glu-Ser(P)-Ile-Ser(P)-Ser(P)-Ser(P)-Glu-Ile-Val-Pro-Asn-Ser(P)-Val-Glu-Gln-Lys<sup>79</sup>[.]  $\alpha_{s1}(59-79)$ ;

(SEQ ID NO: 2) Arg<sup>1</sup>-Glu-[Le8]Leu-Glu-[Iu]Glu-Leu-Asn-Val-Pro-Gly-Glu-Ile-Val-Glu-Ser(P)-Leu-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser-Ile-Thr-Arg<sup>25</sup>[.]  $\beta(I-25)$ ;

(SEQ ID NO: 3) Asn<sup>46</sup>-Ala-Asn-Glu-Glu-Tyr-Ser-Ile-Gly-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser(P)-Ala-Glu-Val-Ala-Thr-Glu-Glu-Val-Lys<sup>70</sup>[.]  $\alpha_{s2}(46-70)$ ; and

(SEQ ID NO: 4) Lys<sup>1</sup>-Asn-Thr-Met-Glu-His-Val-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser-Ile-Ile-Ser(P)-Gln-Glu-Thr-Tyr-Lys<sup>21</sup>[.]  $\alpha_{s2}(1-21)$ .

7. A stable soluble alkaline calcium phosphate complex comprising phosphopeptide-stabilized amorphous calcium phosphate [or a derivative thereof] wherein said phosphopeptide includes the amino acid sequence Ser(P)-Ser(P)-Ser(P)-Glu-Glu (SEQ ID NO: 5) and said amorphous calcium phosphate [or the derivative thereof] is alkaline.

9. A complex according to claim [8] 41, wherein the formula further [including] includes HPO<sub>4</sub><sup>(2-)</sup>.

10. A complex according to claim 9 wherein said phosphopeptide includes an amino acid sequence selected from [any one] the group consisting of:

(SEQ ID NO: 1) Gln<sup>59</sup>-Met-Glu-Ala-Glu-Ser(P)-Ile-Ser(P)-Ser(P)-Ser(P)-Glu-Ile-Val-Pro-Asn-Ser(P)-Val-Glu-Gln-Lys<sup>79</sup>[.]  $\alpha_{s1}(59-79)$ ;

(SEQ ID NO: 2) Arg<sup>1</sup>-Glu-[Le8]Leu-Glu-[Iu]Glu-Leu-Asn-Val-Pro-Gly-Glu-Ile-Val-Glu-Ser(P)-Leu-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser-Ile-Thr-Arg<sup>25</sup>[.]  $\beta(I-25)$ ;

(SEQ ID NO: 3) Asn<sup>46</sup>-Ala-Asn-Glu-Glu-Tyr-Ser-Ile-Gly-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser(P)-Ala-Glu-Val-Ala-Thr-Glu-Glu-Val-Lys<sup>70</sup>[.]  $\alpha_{s2}(46-70)$ ; and

(SEQ ID NO: 4) Lys<sup>1</sup>-Asn-Thr-Met-Glu-His-Val-Ser(P)-Ser(P)-Ser(P)-Glu-Glu-Ser-Ile-Ile-Ser(P)-Gln-Glu-Thr-Tyr-Lys<sup>21</sup>[.]  $\alpha_{s2}(1-21)$ ;

11. A complex according to claim 9 wherein said phosphopeptide includes the amino acid sequence (SEQ ID NO: 1):

Gln<sup>59</sup>-Met-Glu-Ala-Glu-Ser(P)-Ile-Ser(P)-Ser(P)-Ser(P)-Glu-Ile-Val-Pro-Asn-Ser(P)-Val-Glu-Gln-Lys<sup>79</sup> [.]  $\alpha_{s1}(59-79)$ ;

15. (Twice Amended) A method of producing a stable alkaline calcium phosphate complex [according to claim 14 including] having a pH of about 9.0 comprising the steps of:

- (i) [obtaining a solution of phosphopeptide having a pH of about 9.0;]  
obtaining an aqueous solution of a phosphopeptide which has a pH of about 9.0,  
wherein said phosphopeptide includes the amino acid sequence Ser(P)-Ser(P)-Ser(P)-Glu-Glu (SEQ ID NO: 5);
- (ii) admixing the solution of step (i) with solutions comprising calcium, and inorganic phosphate and optionally fluoride at a pH of about 9.0;
- (iii) filtering the mixture resulting from step (ii)[,]; [and]
- (iv) drying [to obtain the said complex] the mixture of step (iii), and
- (v) isolating the stable alkaline calcium phosphate complex .

25. (Amended) A method of [treating or preventing] inhibiting dental caries or tooth decay [including] comprising [the step of] administering a complex according to claim [1] 7 to the teeth or gums of a subject in need of such treatment.